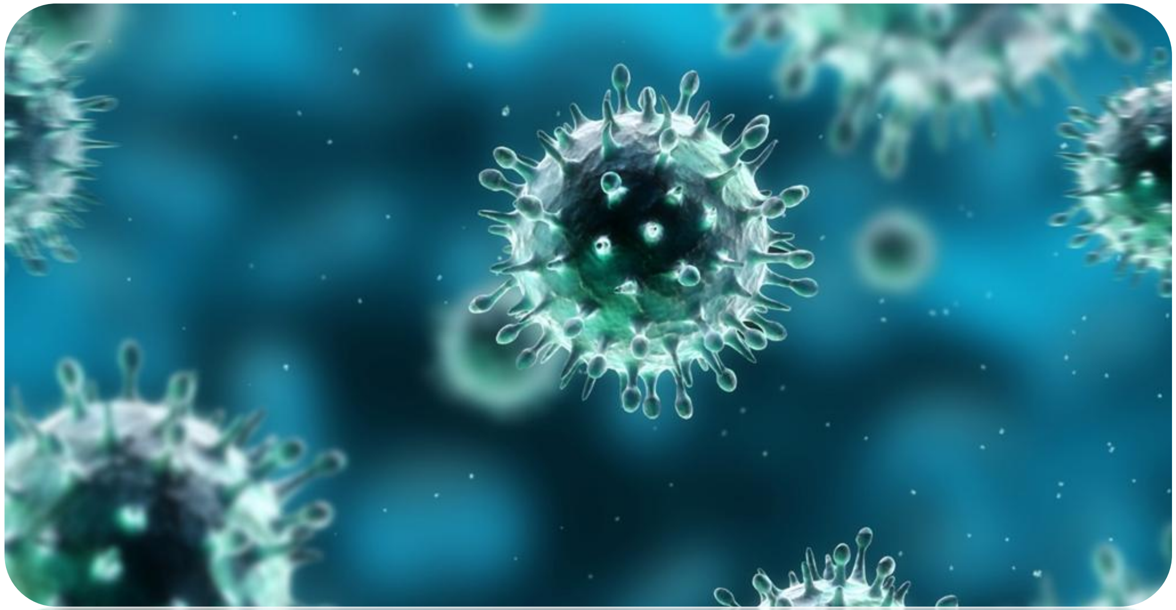
Chapter two A: Virus structure



علم الفيروسات لطلبة التحاليل الطبية
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Table 10.1 Some milestones in the history of virology

1892	Tobacco Mosaic Disease (TMD) shown to be caused by a filterable agent.	Iwanowsky
1898	Proposal that TMD is due to a novel type of infectious agent.	Beijerinck
	Demonstration of first viral disease in animals (foot and mouth).	Loeffler & Frosch
1901	Demonstration of first human viral disease (yellow fever).	Reed
1915/1917	Discovery of bacterial viruses (bacteriophages).	Twort, d'Herelle
1918	Spanish influenza pandemic	
1935	TMV is first virus to be crystallised.	Stanley
1937	Separation of TMV into protein and nucleic acid fractions.	Bawden & Pirie
1939	Viruses visible under electron microscope	Kausche, Pfankuch & Ruska
1955	Spontaneous reassembly of TMV from protein and RNA components.	Fraenkel-Conrat & Williams

1971	Discovery of viroids.	Diener
1980	Sequencing of first complete viral genome (CaMV)	Frank
1982	Sequencing of first RNA genome (TMV)	
	Recombinant Hepatitis B vaccine	
	Discovery of prions	Prusiner
1983	Discovery of HIV, thought to be causative agent of AIDS	Montaigner and Gallo
1990	Retrovirus used as vector in first human gene therapy trial.	Anderson
2001	BSE outbreak in UK	
2003	Outbreak of new human viral disease (SARS) in SE Asia	

TMV, Tobacco mosaic virus; CaMV, Cauliflower mosaic caulimovirus.

Introduction to virus structure

- Outside their host cells, viruses survive as virus particles, also known as virions.

- The virion is a gene delivery system; it contains the virus genome, and its functions are to protect the genome and to aid its entry into a host cell, where it can be replicated and packaged into new virions.

- The genome is packaged in a protein structure known as a capsid.

- Many viruses also have a lipid component, generally present at the surface of the virion forming an envelope, which also contains proteins with roles in aiding entry into host cells.

Virus genomes

- A virion contains the genome of a virus in the form of one or more molecules of nucleic acid. For any one virus the genome is composed of either RNA or DNA.

- If a new virus is isolated, one way to determine whether it is an RNA virus or a DNA virus is to test its susceptibility to a ribonuclease and a deoxyribonuclease.

- The virus nucleic acid will be susceptible to degradation by only one of these enzymes

Virus genomes

- Each nucleic acid molecule is either single-stranded (ss) or double-stranded (ds), giving four categories of virus genome: dsDNA, ssDNA, dsRNA and ssRNA.

- The dsDNA viruses encode their genes in the same kind of molecule as animals, plants, bacteria and other cellular organisms, while the other three types of genome are unique to viruses.

- It interesting to note that most fungal viruses have dsRNA genomes, most plant viruses have ssRNA genomes and most prokaryotic viruses have dsDNA genomes.

Virus genomes

- A further categorization of a virus nucleic acid can be made on the basis of whether the molecule is linear, with free 5′ and 3′ ends, or circular, as a result of the strand(s) being covalently closed.

DNA genomes

		Examples
	ss, linear	Parvoviruses
	ds, linear	Poxviruses
	ss, circular	Phage φX174
	ds, circular	Baculoviruses

RNA genomes

	ss, linear	Tobacco mosaic virus
	ds, linear	Reoviruses
	ss, circular	Hepatitis delta virus

Virus genomes

Genome size

- Virus genomes span a large range of sizes. Porcine circovirus (ssDNA) and hepatitis delta virus (ssRNA) each have a genome of about 1.7 kilobases (kb), while at the other end of the scale there are viruses with dsDNA genomes comprised of over 1000 kilobase pairs (kbp).

- All of the large virus genomes are composed of dsDNA.
- The largest RNA genomes known are those of some coronaviruses, which are 33 kb of ssRNA.

- The largest virus genomes, such as that of the mimivirus, are larger than the smallest genomes of cellular organisms, such as some mycoplasmas

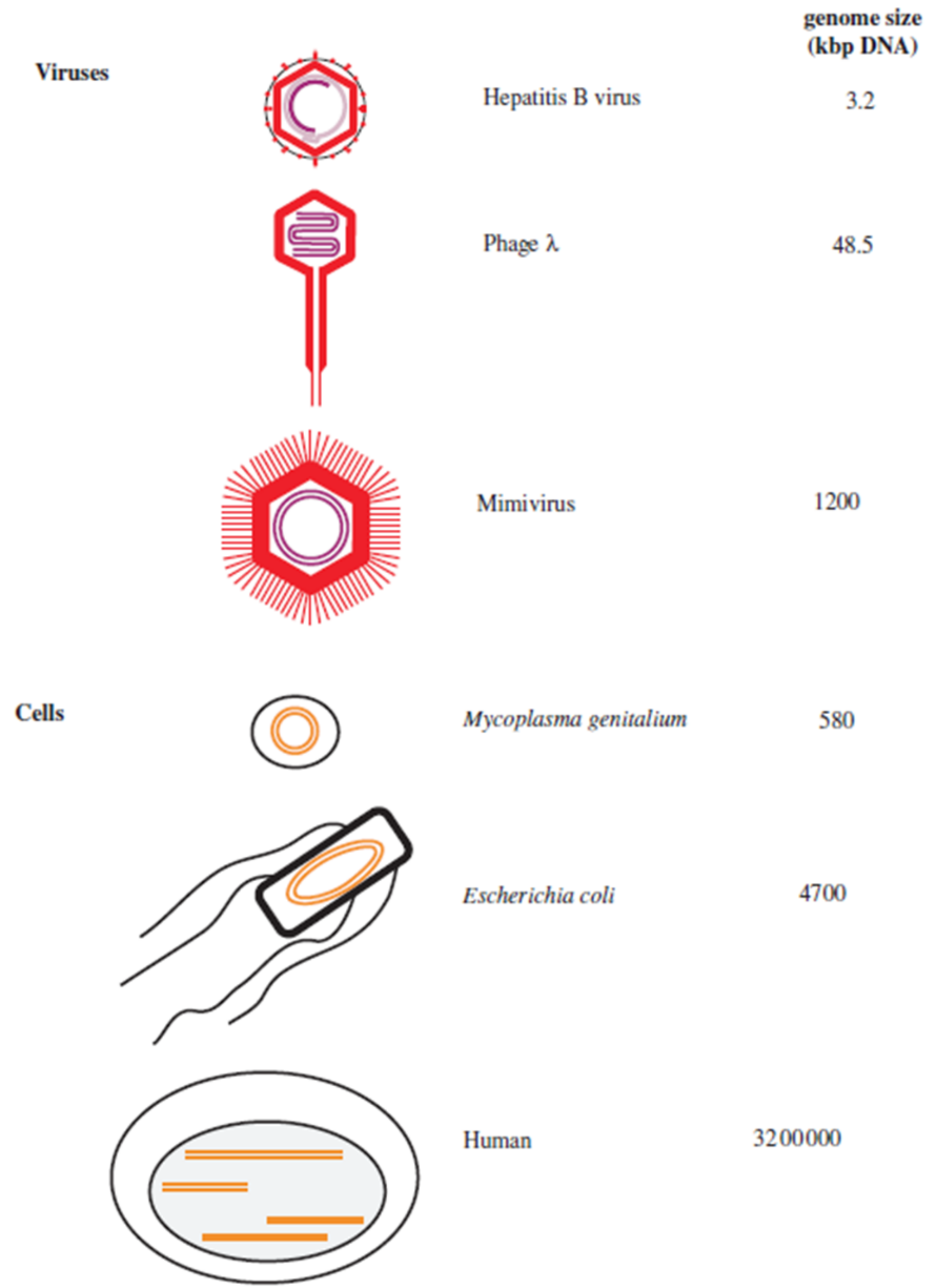


Figure 3.2 Genome sizes of some DNA viruses and cells. Not to scale.

Virus genomes

Proteins non-covalently associated with virus genomes

- Many nucleic acids packaged in virions have proteins bound to them non-covalently.

- These proteins have regions that are rich in the basic amino acids lysine, arginine and histidine, which are negatively charged and able to bind strongly to the positively charged nucleic acids.

- Papillomaviruses and polyomaviruses, which are DNA viruses, have cell histones bound to the virus genome.

Virus genomes

Segmented genomes

- Most virus genomes consist of a single molecule of nucleic acid, but the genes of some viruses are encoded in two or more nucleic acid molecules.

- These segmented genomes are much more common amongst RNA viruses than DNA viruses. Examples of ssRNA viruses with segmented genomes are the influenza viruses which package the segments in one virion.

- The possession of a segmented genome provides a virus with the possibility of new gene combinations, and hence a potential for more rapid evolution

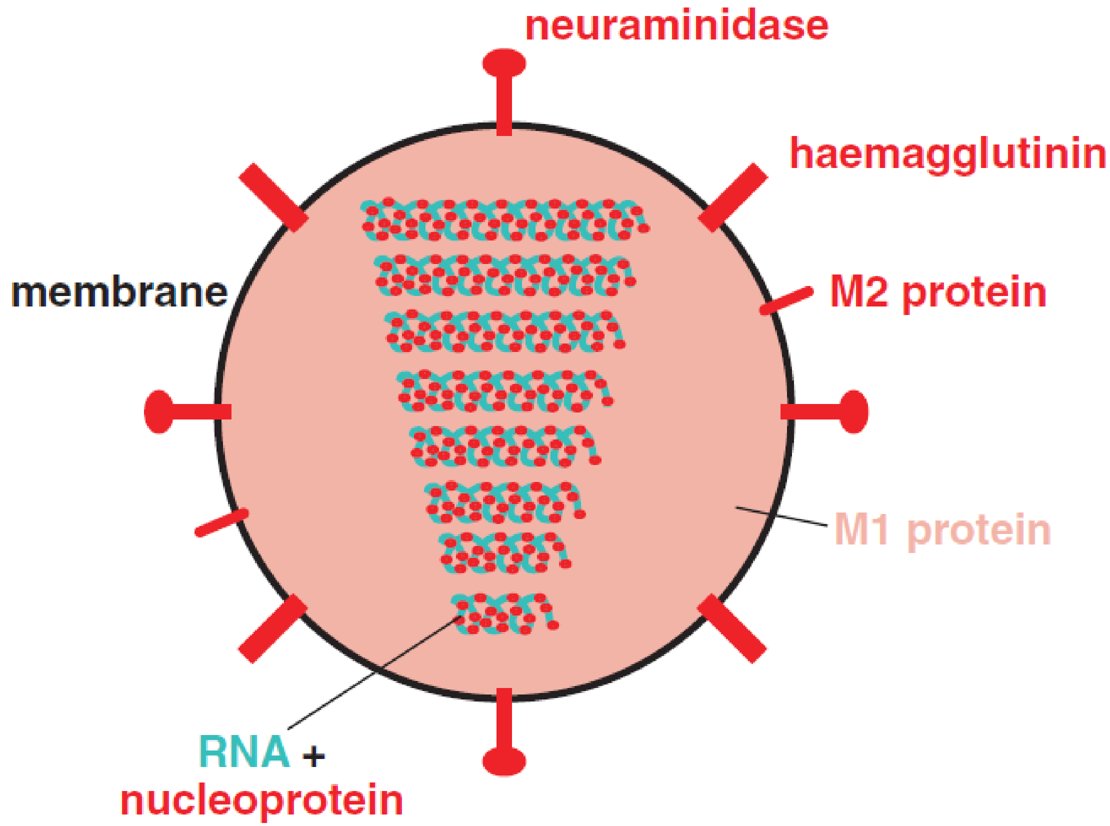


Figure 3.20 *Influenza A virus.* The envelope contains two species of glycoprotein (haemagglutinin and neuraminidase) and a non-glycosylated protein (M2). Underlying the envelope is a layer of M1 (membrane or matrix) protein, which encloses the helical nucleocapsid (eight segments of ssRNA coated with nucleoprotein) and several other proteins.

Virus proteins

- The virion of tobacco mosaic virus contains only one protein species and the virions of parvoviruses contain two to four protein species. These are viruses with small genomes.

- As the size of the genome increases, so the number of protein species tends to increase; 39 protein species have been reported in the virion of herpes simplex virus 1, and over 100 in the virion of the algal virus *Paramecium bursaria Chlorella* virus 1.

Virus proteins

- Proteins that are components of virions are known as structural proteins. They have to carry out a wide brange of functions, including

  - ✓ • Protection of the virus genome
  - ✓ • Attachment of the virion to a host cell
  - ✓ • Fusion of the virion envelope to a cell membrane (for enveloped viruses)..

Virus proteins

- Virus proteins may have additional roles, some of which may be carried out by structural proteins, and some by non-structural proteins (proteins synthesized by the virus in an infected cell but they are not virion components).

- These additional roles include
  - enzymes, e.g. protease, reverse transcriptase
  - transcription factors
  - primers for nucleic acid replication
  - interference with the immune response of the host

Virus proteins

Nomenclature of virus proteins

- There is no standard system of nomenclature for virus proteins, with different systems having evolved for different groups of viruses. For quite a number of viruses the following system has been adopted, the proteins being numbered in decreasing order of size:

  - structural proteins VP1, VP2, VP3, .. (VP = virus protein)
  - non-structural proteins: NSP1, NSP2, NSP3,

Many virus proteins are known by an abbreviation of one or two letters, which may indicate

- a <u>structural characteristic</u> **G** (glycoprotein) **P** (phosphoprotein) or a <u>function</u> **F** (fusion) **P** (polymerase) **RT** (reverse transcriptase).

Capsids

- Virus genomes removed from their capsids are more susceptible to inactivation, so a major function of the capsid is undoubtedly the **protection** of the genome.

- A second major function of many capsids is to **recognize** and **attach** to a host cell in which the virus can be replicated.

- Capsids are constructed from many molecules of one or a few species of protein. The individual protein molecules are asymmetrical, but they are organized to form **symmetrical** structures.

- For the vast majority of viruses the capsid symmetry is either **helical** or **icosahedral**

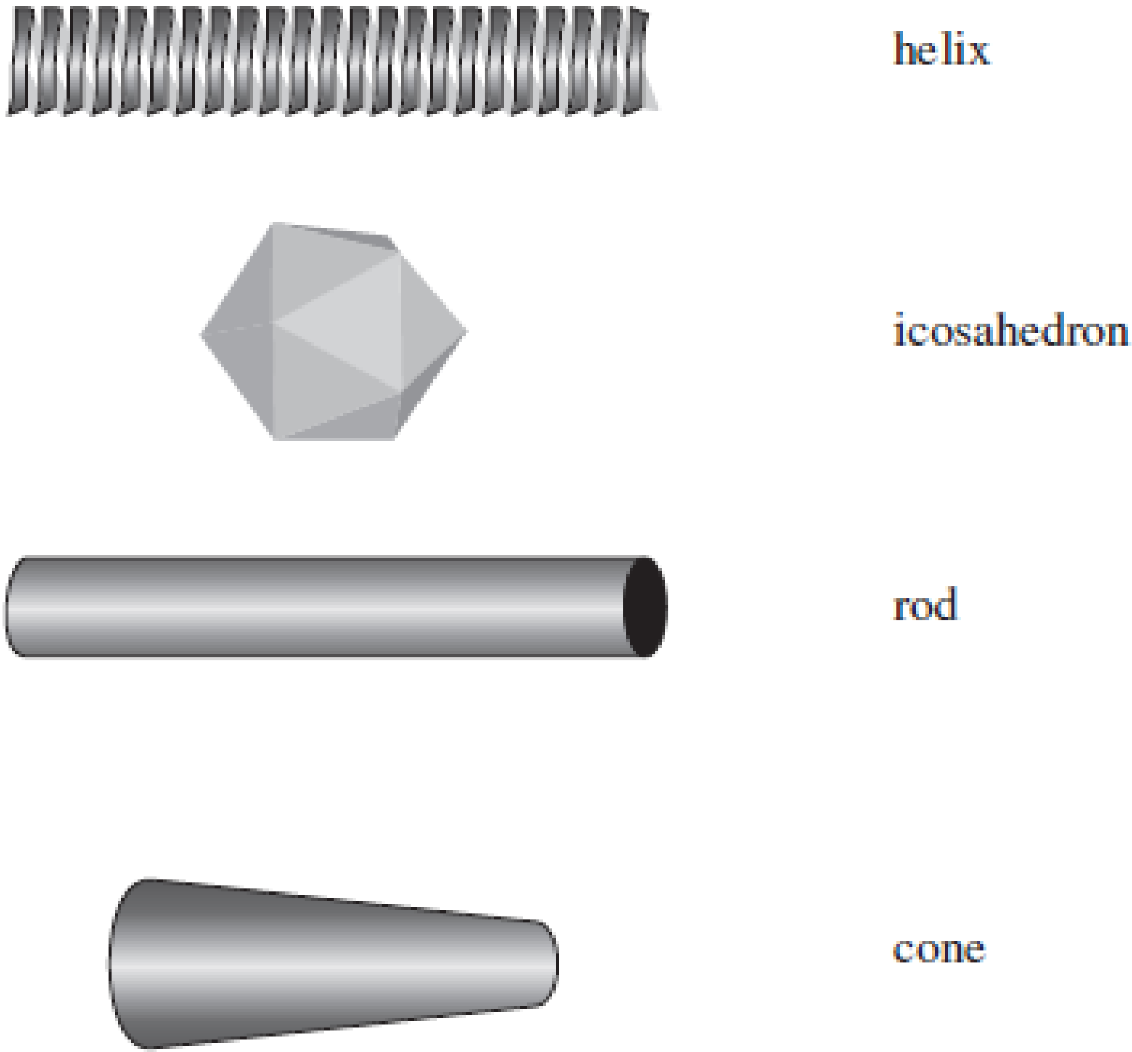


Figure 3.8 **Symmetrical structures.** All these types of symmetry are seen amongst viruses. The most common are helical and icosahedral symmetries.

Capsids with helical symmetry

- The capsids of many ssRNA viruses have helical symmetry.
- The RNA is coiled in the form of a helix and many copies of the same protein species
- These protein are arranged around the coil (Figure 3.9(a), (b)). This forms an elongated structure, which may be a **rigid rod** if strong bonds are present between the protein molecules in successive turns of the helix, or a **flexible rod** (Figure 3.9(c)) if these bonds are weak.

- The length of the capsid is determined by the length of the nucleic acid.

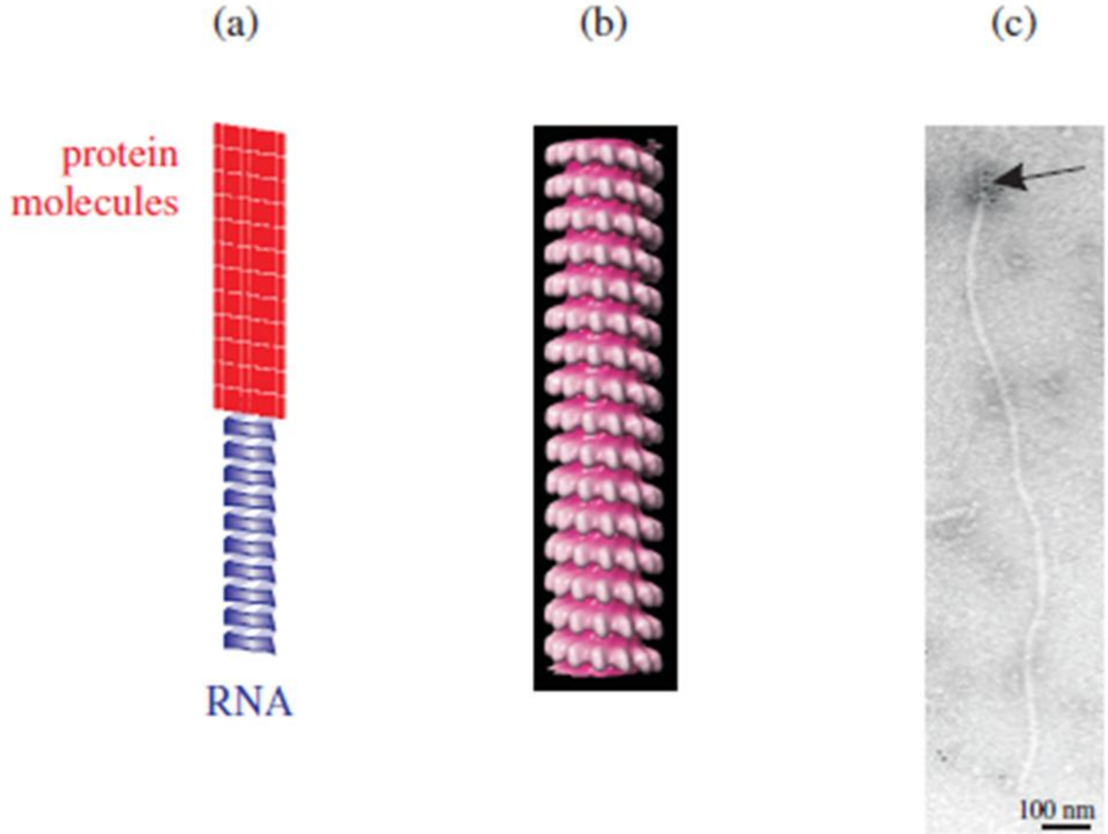


Figure 3.9 Helical symmetry. (a) Structure of a capsid with helical symmetry. The ssRNA coil is coated with repeated copies of a protein. (b) Part of measles virus nucleocapsid. The complete nucleocapsid is folded and enclosed within an envelope. (c) Beet yellows virus particle. The virion is a long flexible rod, at one end of which there is a "tail" (arrow) composed of a minor capsid protein, detected here by specific antibodies labeled with gold.

Capsids with helical symmetry

- For many ssRNA viruses, such as measles and influenza viruses, the helical nucleic acid coated with protein forms a nucleocapsid, which is inside an envelope (see Figure 3.20).

- The nucleocapsid may be coiled or folded to form a compact structure.

- The virions of some plant viruses that have helical symmetry (e.g. tobacco mosaic virus) are hollow tubes.

- The virions of a few DNA viruses, such as the filamentous phages , also have helical symmetry.

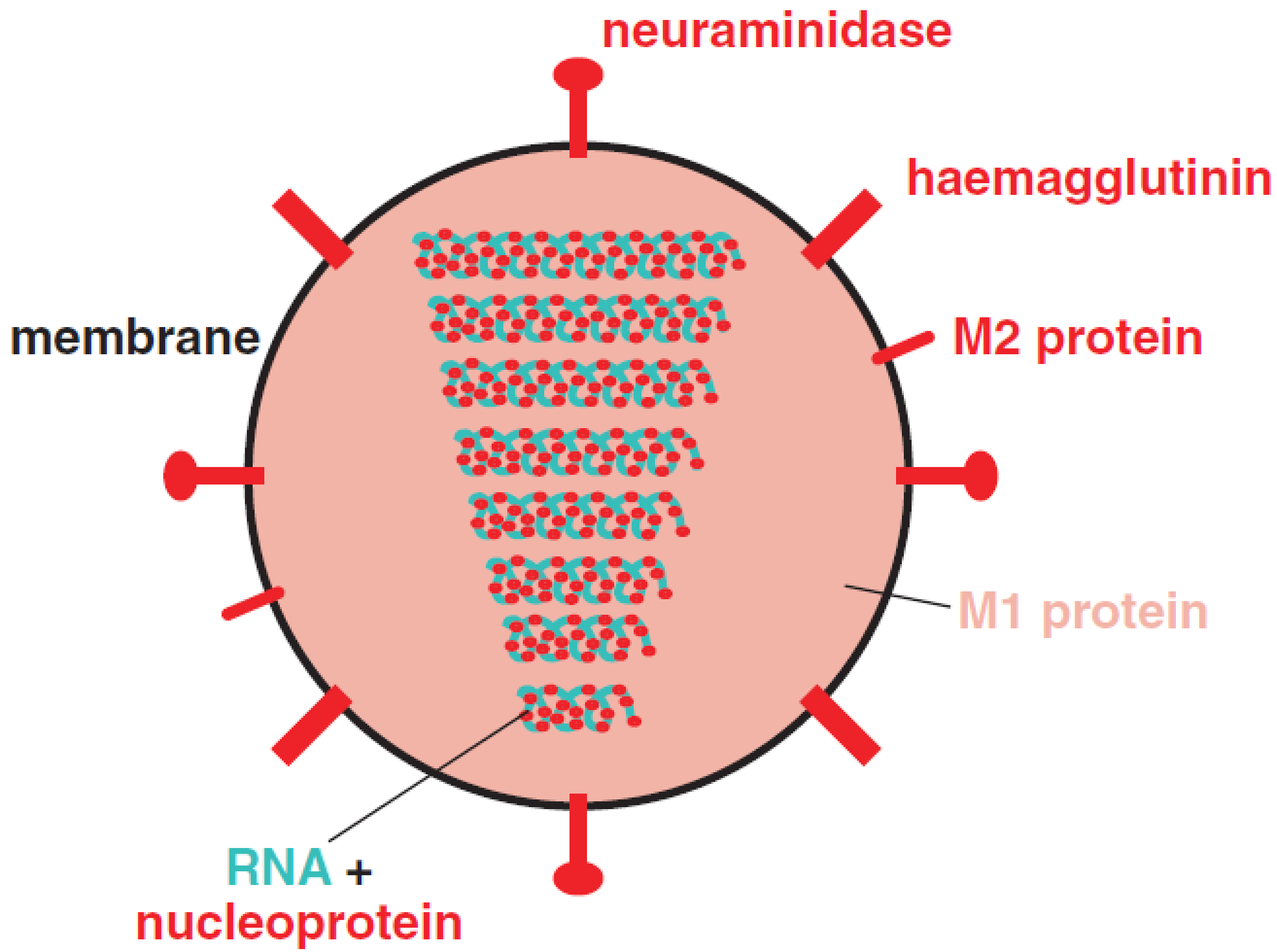


Figure 3.20 *Influenza A virus*. The envelope contains

Capsids with icosahedral symmetry

What does icosahedron mean ?

An icosahedron is an object with

- • 20 faces, each an equilateral متساوي الاضلاع triangle;
- • 12 vertices قمة مدببه , each formed where the vertices of five triangles meet;
- • 30 edges, at each of which the sides of two triangles
- meet.

Capsids with icosahedral symmetry

- An icosahedron has five-, three- and two-fold axes
- of rotational symmetry (Figure 3.10).
- Capsids with icosahedral symmetry consist of a shell built from protein molecules that appear to have been arranged on scaffolding in the form of an icosahedron.
- They have less contact with the virus genome than the capsid proteins of viruses with helical symmetry.

- To construct an icosahedron from identical protein molecules the minimum number of molecules required is three per triangular face, giving a total of 60 for the icosahedron

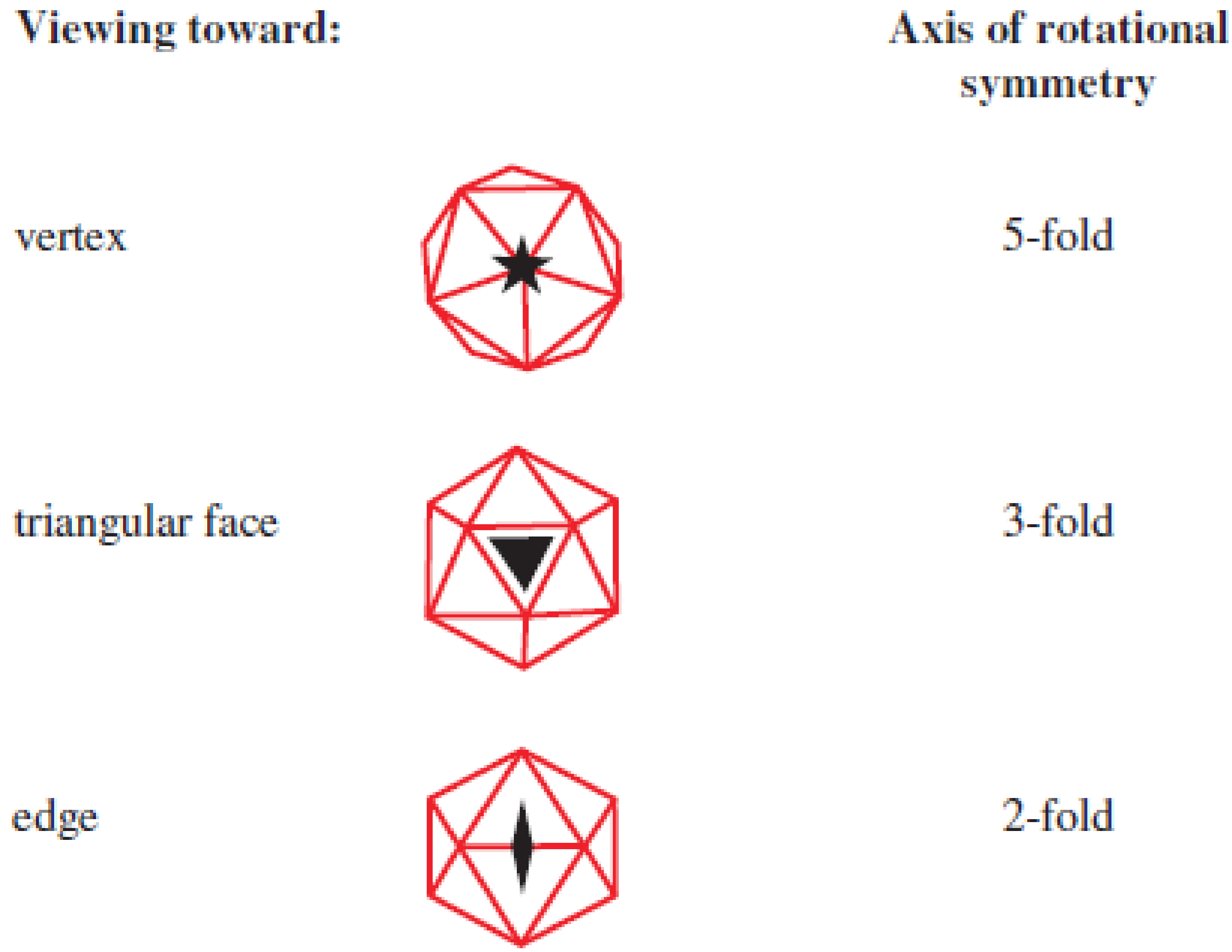


Figure 3.10 The three axes of symmetry of an icosahedron.

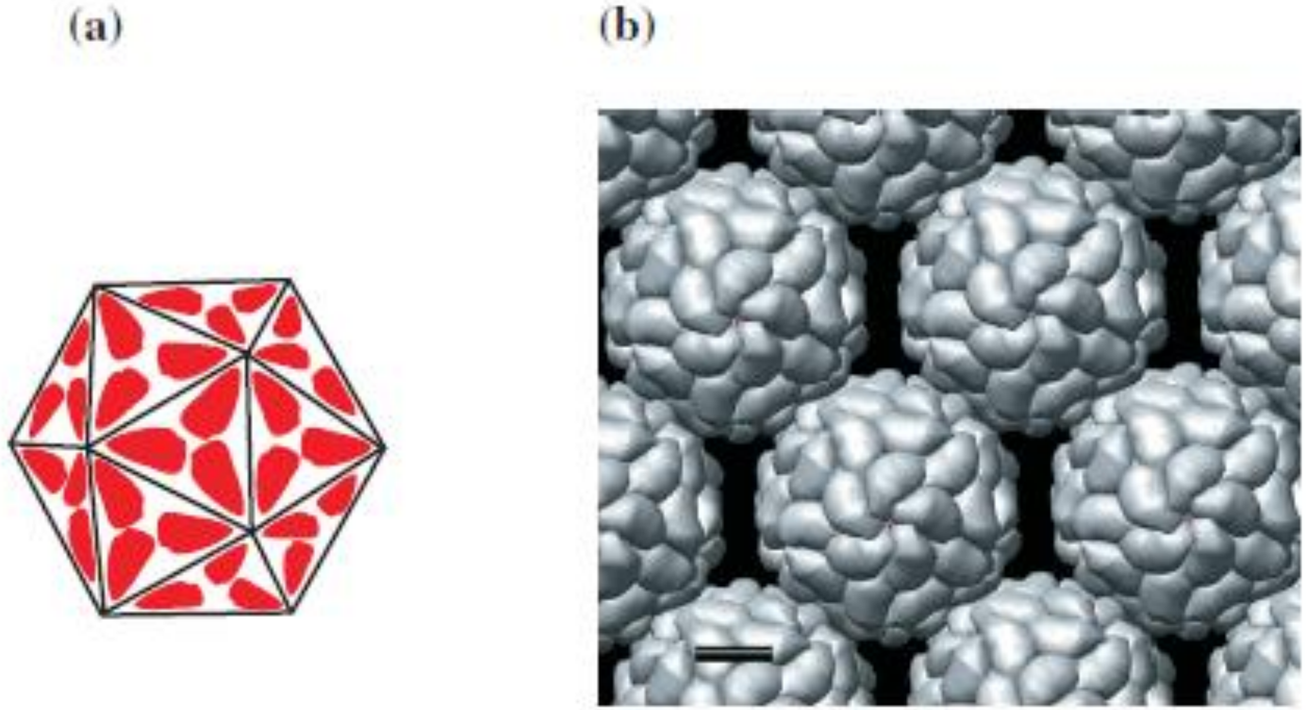


Figure 3.11 Capsid constructed from sixty protein molecules. (a) Arrangement of protein molecules, with three per triangular face. (b) Virions of satellite tobacco mosaic virus. The bar represents 5 nm. Image created with the molecular graphics program UCSF Chimera from the Resource for Biocomputing, Visualization, and Informatics, at the University of California, San Francisco.

Source: Courtesy of Tom Goddard.

Capsids with icosahedral symmetry

- The capsids of many icosahedral viruses are composed of more than one protein species.

- **cowpea mosaic virus** is composed of two proteins (Figure 3.12): one is present as ‘pentamers’ at the vertices of the icosahedron ($12 \times 5 = 60$ copies) and the other is present as ‘hexamers’ on the faces.

- Each ‘hexamer’ is composed of three copies of a protein with two domains. The arrangement is similar to that of the panels on the surface of the football in Figure 3.12.

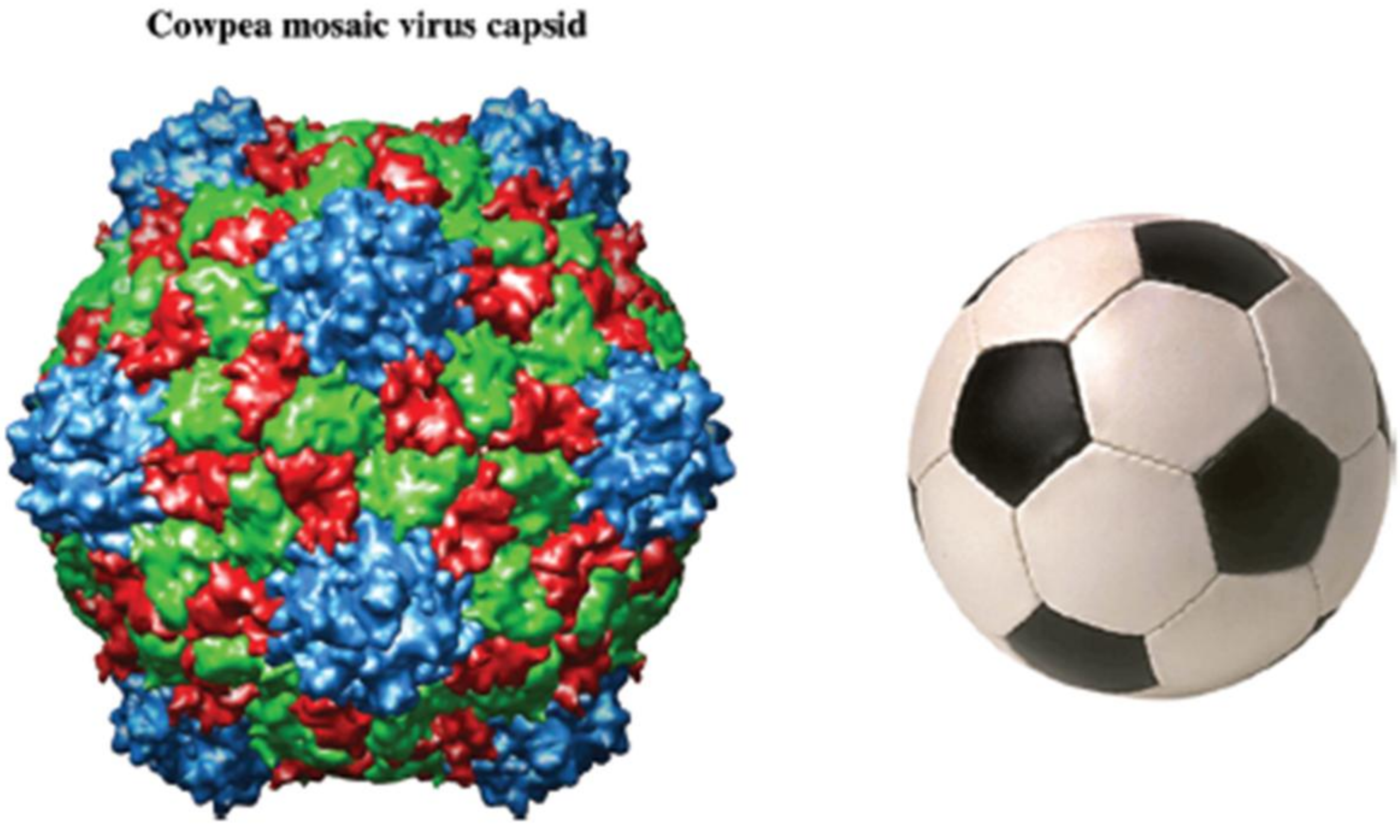


Figure 3.13 Capsid constructed from two protein species. The cowpea mosaic virus capsid is constructed from one protein species (blue) that forms 12 “pentamers,” and from a second protein species with two domains (green and red) that forms 20 “hexamers.” The football is similarly constructed from 12 “pentamers” and 20 “hexamers.” The cowpea mosaic virus image is from the VIPER database

Capsids with icosahedral symmetry

- There is also a huge range in the sizes of icosahedral capsids.
- The *satellite tobacco mosaic* virus capsid is about 17 nm in diameter, whereas the diameter of the *Paramecium bursaria Chlorella* virus 1 capsid is about ten times greater than this (Figure 3.13)
-
- The mimivirus capsid is about 300 nm in diameter

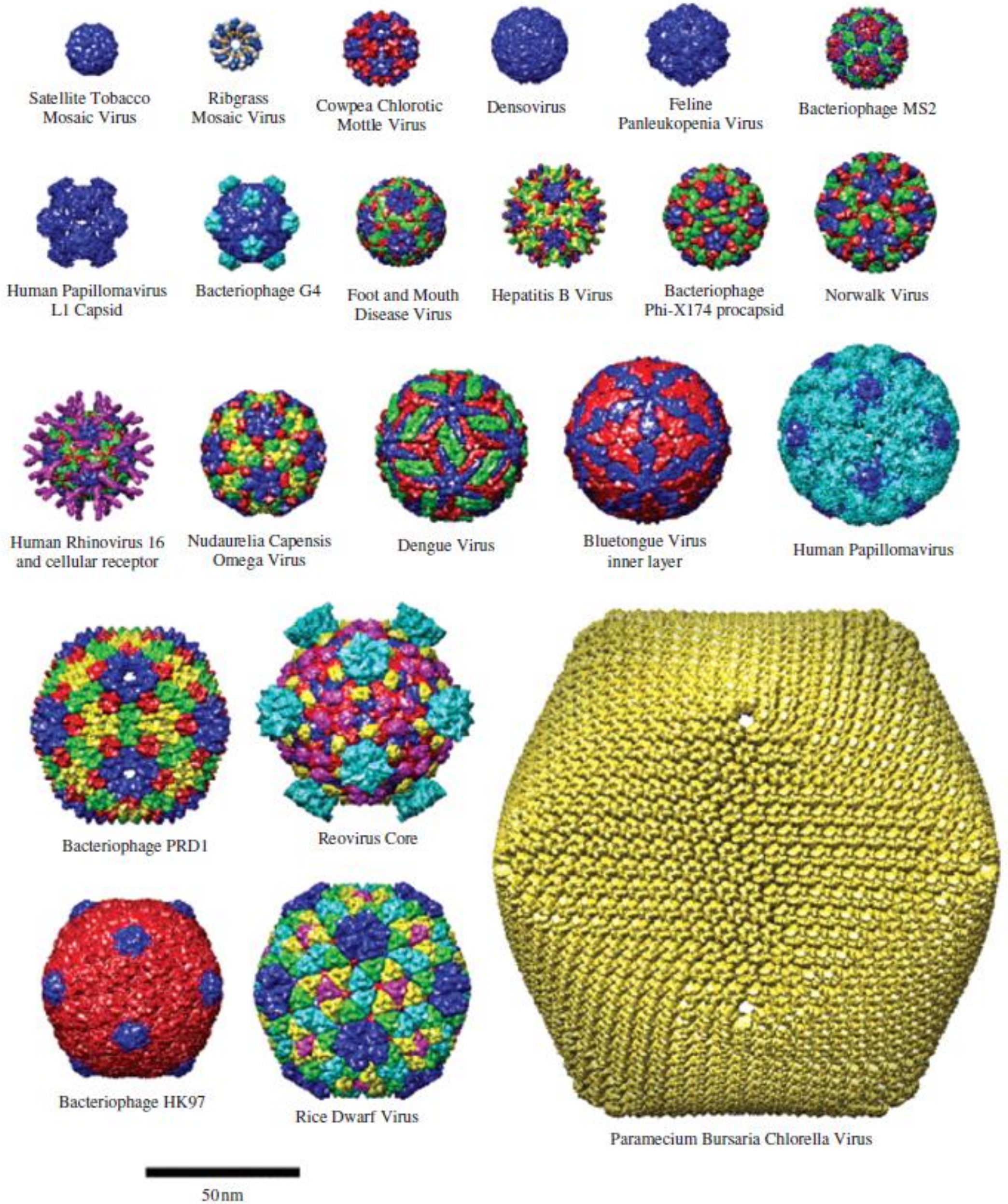
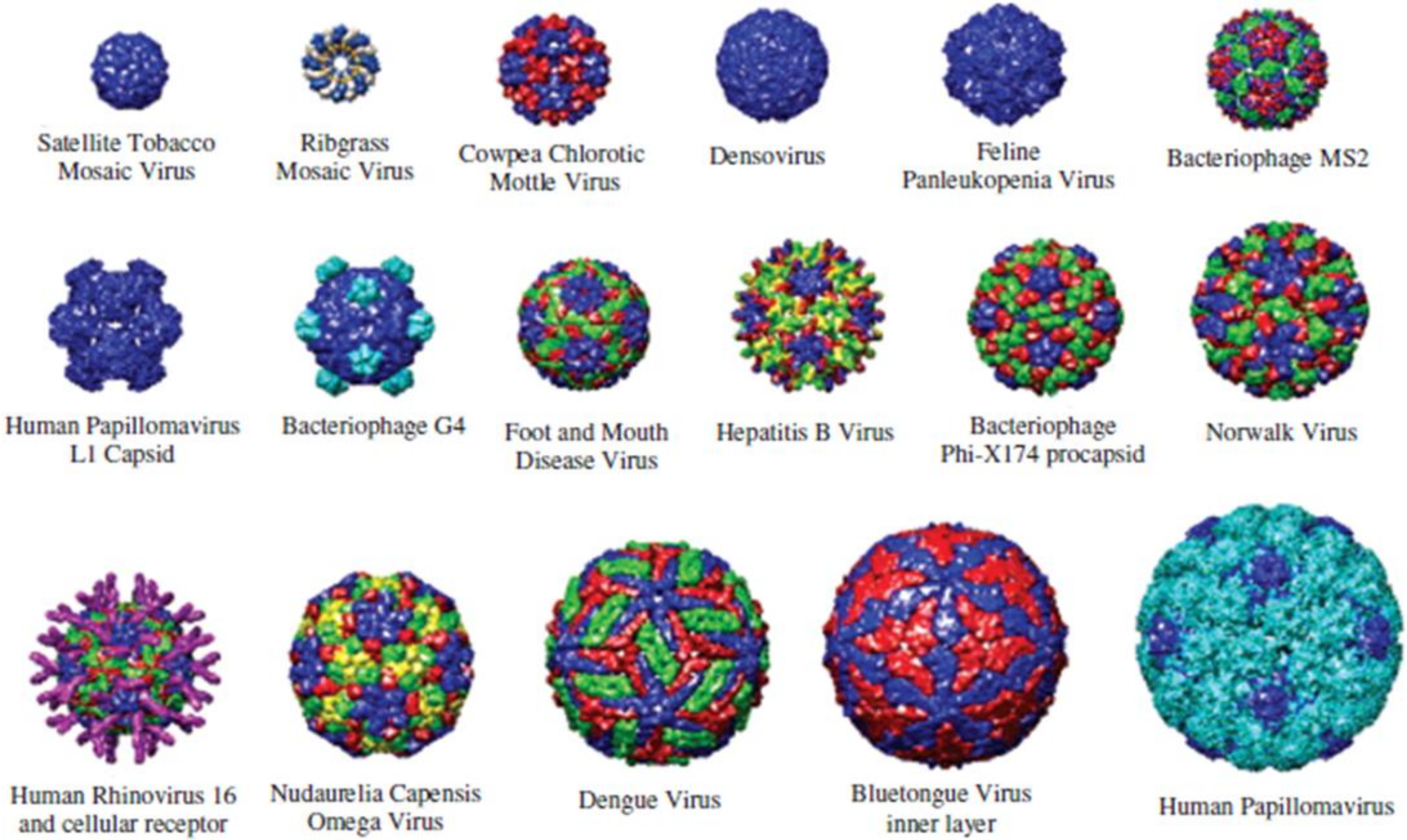
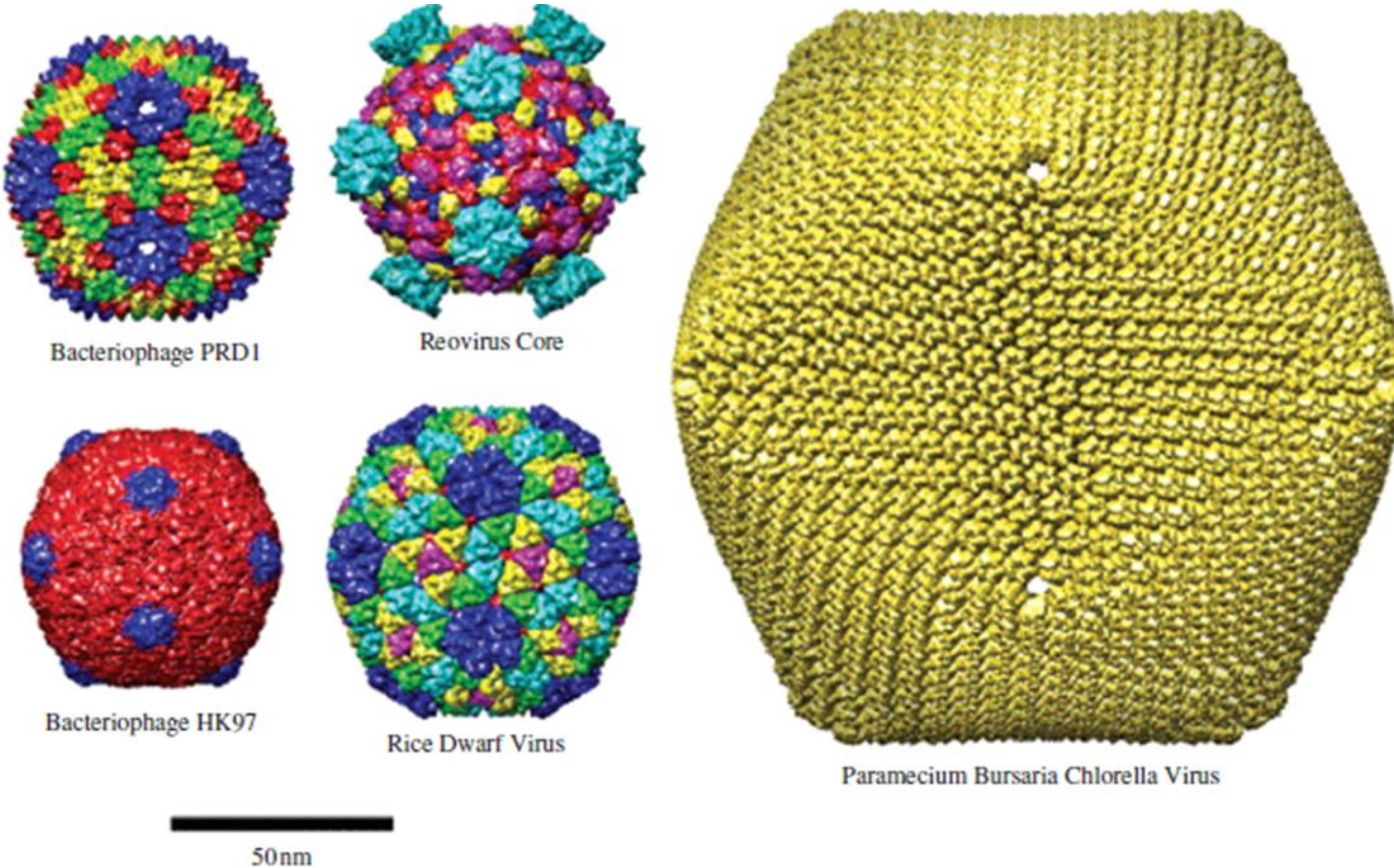


Figure 3.14 Capsids with icosahedral symmetry. Some of the wide ranges of capsid architectures and sizes are illustrated. The images were created with the molecular graphics program UCSF Chimera using data from cryo-electron microscopy and X-ray diffraction.

Source: Goddard *et al.* (2005) *Structure*, 13, 473. Reproduced by permission of Elsevier Limited.


Satellite Tobacco Mosaic Virus
Ribgrass Mosaic Virus
Cowpea Chlorotic Mottle Virus
Densovirus
Feline Panleukopenia Virus
Bacteriophage MS2
Human Papillomavirus L1 Capsid
Bacteriophage G4
Foot and Mouth Disease Virus
Hepatitis B Virus
Bacteriophage Phi-X174 procapsid
Norwalk Virus
Human Rhinovirus 16 and cellular receptor
Nudaurelia Capensis Omega Virus
Dengue Virus
Bluetongue Virus inner layer
Human Papillomavirus


Bacteriophage PRD1
Reovirus Core
Paramecium Bursaria Chlorella Virus
Bacteriophage HK97
Rice Dwarf Virus
50nm

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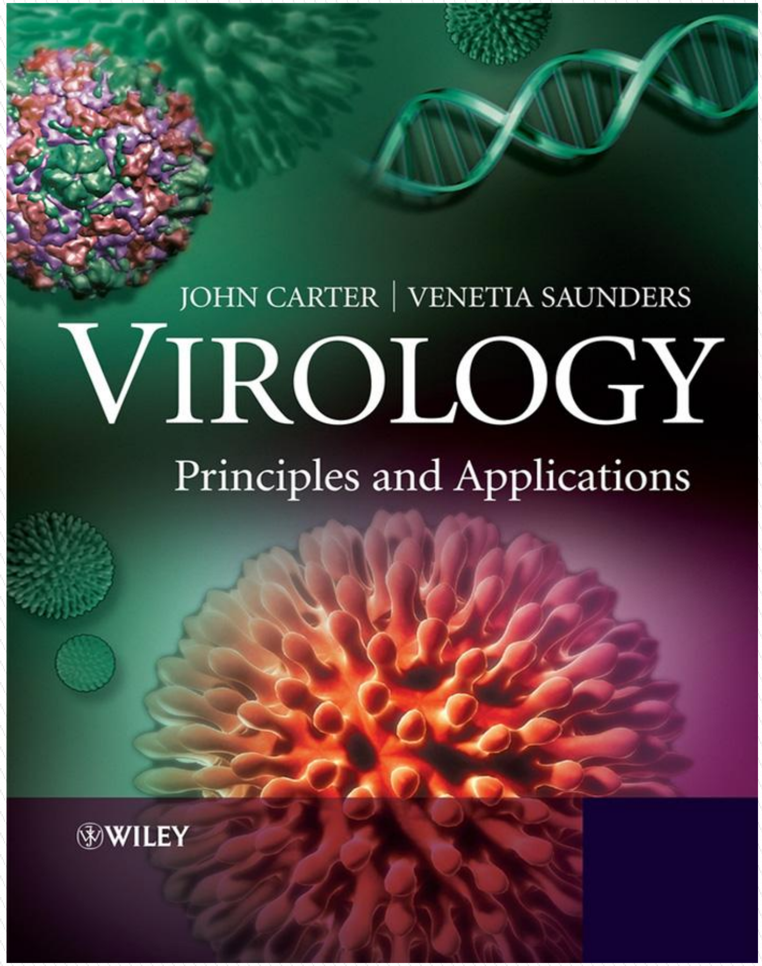

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